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Short Communication

Invitro susceptibility test of *Candida* spp. isolates from pulmonary tuberculosis suspected patients to antifungal agents in Jakarta

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Pulmonary infection is still a major health concern in Indonesia, and fungal infection is emerging. This may be related to widely used broad spectrum antibiotics, steroids, oral contraceptive, cytostatic, and chronic diseases.The aim of this study was to describe *Candida* spp sensitivity pattern to various antifungal agents from pulmonary tuberculosis suspected patients. In this study, we used 176 sputum samples from tuberculosis suspected patients. The samples were cultured 3 times in Sabouraud dextrose agar. Yeast was identified by API 20 C AUX, while antifungal susceptibility test used ATB FUNGUS 3. There were 85 samples infected by yeast. As many as 74 isolates were identified as *C. albicans* (87.1%), 9 isolates were *C. tropicalis* (10.6%) and 2 were *C. dubliniensis* (2.4%). The susceptibility test showed six isolates of *C. albicans* and one isolate of *C. tropicalis* were intermediate against itraconazole. Only three isolates of *C. albicans* were resistant against itrazonazole, fluconazole, and voriconazole. Fortunately, they were still sensitive to amphotericine B and flucytosine. Almost half of tuberculosis suspected patients were infected by *Candida* spp. Most of them were still sensitive to various antifungal agents, although few *C. albicans* isolates were resistant against fluconazole, itraconazole, voriconazole.

Keywords: Fungal infection, tuberculosis, *Candida* spp, antifungal susceptibility.

INTRODUCTION

Fungal pulmonary infection has been emerging recently due to widely used broad spectrum antibiotics and steroids (Nucci and Marr, 2005). It can be acquired primarily or secondarily in tuberculosis, immunodeficiency patients, other chronic diseases such as diabetes mellitus or malignancy, and may worsen the primary disease (Baradkar et al., 2009; Ozcelik et al., 2004; Kovacicova et al., 2000; Satana et al., 2010; Basu et al., 2010) Many physicians missed fungal pulmonary infection because it doesn't show specific clinical manifestations and usually hindered by other diseases (Pfaller and Diekema, 2007). Therapeutic approach to fungal pulmonary infection has become attention due to several cases of resistance against antifungal agents (Dimopoulos et al., 2009; Lyon et al., 2010).

METHODS

The samples were taken consecutively from April 2009 to August 2010 from two hospitals and two primary health care facilities in Jakarta The participants were pulmonary tuberculosis suspected patients. The inclusion criteria were: age ≥15 year old suspected pulmonary tuberculosis that fulfilled at least two of these symptoms: cough for ≥2 weeks, hemoptysis, dyspnoe, chest pain, night sweat, fever, weight loss. Sputum was collected within three consecutive days in the morning. Samples were excluded if participants denied to sign the informed consent, cannot collect three sputum samples conse-

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Table 1. Patients' characteristic

Sample		
Patients	**Number**	**%**
Age group (years)		
15-19	2	1.1
20-29	29	6.5
30-39	26	14.8
40-49	40	22.7
50-59	44	25.0
60-69	16	9.1
> 70	19	10.8
Sex		
Male	108	61.5
Female	68	38.6

n = 176

Table 2. Sensitivity pattern of *Candida* spp to flucytosine, amphotericin, fluconazole, itraconazole and voriconazole

Species (number of isolates)	**Antifungal agents**	**Sensitive(%)**	**Intermediate(%)**	**Resistant (%)**
Candida albicans (74)	flucytosine	74(100)		
	amphotericin B	74(100)		
	fluconazole	71(95.9)		3(4.1)
	itraconazole	65(87.8)	6(8.1)	3(4.1)
	voriconazole	71(95.9)		3(4.1)
C. tropicalis (9)	flucytosine	9(100)		
	amphotericin B	9(100)		
	fluconazole	9(100)		
	itraconazole	8(88.9)	1(11.1)	
	voriconazole	9(100)		
C. dublienensis	flucytosine	2(100)		
	amphotericin B	2(100)		
	fluconazole	2(100)		
	itraconazole	2(100)		
	voriconazole	2(100)		

cutively, and the culture result revealed mold. Sputum was collected from 176 suspected pulmonary tuberculosis patients after informed consent.

The samples were examined three times by cultured in Sabouroud dextrose agar. If the culture had given positive result, it was then identified for yeast by API 20 C AUX (bioMerieux S.A Marcy-1"Etoile France, 2007) and sensitivity test against antifungals by ATB FUNGUS 3 (bioMerieux S.A Marcy-1"Etoile France, 2007). The examination fulfilled the standard of CLSI, document M27-A3 (Clinical and Laboratory Standars Institute(CLSI). Reference method for broth dilution antifungal susceptibility testing of yeasts, 3rd ed Approved standard CLSI M27-A3 Clinical and Laboratory Standards Institute, Wayne, PA 2008).

RESULTS AND DISCUSSIONS

There were 108 men, age ranged 25-78 years old (mean 53 years old), and 68 wome, age 19-76 years old (mean 48 years old) (table 1).

From 176 samples, 97 (55.1%) were fungi (12 molds and and 85 yeasts) and 79 were negative. As listed in table 2, from 85 (48.3%) yeasts isolates, most of them were *C. albicans*, followed by *C. tropicalis*, and *C. dubli-*

niensis. Table 2 also shows sensitivity test of *Candida* spp against antifungal regimens.

Six isolates of *C. albicans* and one isolate of *C. tropicalis* gave intermediate results against itraconazole. Only three isolates, all were *C. albicans*, were resistant against fluconazole, itraconazole, and voriconazole.

About 55.1% of the samples were infected by fungi. Study by Suryatenggara et al in 1995 found less, that was about 45% of bronchial wash samples infected by fungi (Suryatenggara et al., 1995). Baradkar et al[6] reported 26% tuberculous patients were infected by yeast, much less than 48.3% found in our study. Frequent and irrationale antibiotic use, especially broad spectrum, was considered the cause of this phenomen.

From all the yeast isolated, most of them were *C. albicans*, *C. tropicalis*, *and C. dubliniensis*. Study by Baradkar et al., 2009; Jha et al., 2006; Basu et al., 2003, and Makaddas et al., 2005 also reported that *C. albicans* was the most frequent yeast isolated.

All of *Candida* spp in this study were still sensitive to flucytosine and amphotericine B. This is in accordance with study by Fleck et al, which may be caused by seldom use of the drugs (Fleck et al., 2005). On the other hand, some of *C. tropicalis* and *C. albicans* gave intermediate and resistant results to itraconazole and fluconazole, maybe because the drugs are more frequently used in community.

CONCLUSION

In this study, almost half of tuberculosis suspected patients were infected by *Candida* spp. Most of them were still sensitive to various antifungal agents, although few *C. albicans* isolates were resistant against fluconazole, itraconazole, voriconazole. This may lead us to consideration of trend toward increasing resistance rate of *Candida* spp against antifungal agents.

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